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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,665	09/07/2004	Beka Solomon	SOLOMON6A	5010

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EXAMINER	
BALLARD, KIMBERLY A	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 11/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/506,665	SOLOMON, BEKA	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/7/04, 7/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

Applicant's amendment to the claims filed September 22, 2006 has been entered. Applicant has cancelled claims 16-22. Claims 1-15 are pending in the instant application.

Election/Restrictions

Applicant's election of Group I, claims 1-15, in the reply filed on September 22, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims **1-15** are under examination in the instant office action.

Specification

The disclosure is objected to because of the following informalities: there appears to be typographical error in the sequence listing for SEQ ID NO: 1 in which amino acid residues 22 and 23 appear to be switched. The specification states that SEQ ID NO: 1 is the amino acid sequence surrounding the β-secretase site on AβPP (see [0031]). The instant sequence listing discloses these residues as Leu22 and Lys23. The examiner notes the sequence for AβPP is well recognized in the art, and the art specifies these residues as Lys22 and Leu23. Appropriate correction is required.

Sequence Requirements

In order to have compact prosecution a first office action can be performed on this application, however, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. The disclosure contains sequences that need sequence identifier numbers (SEQ ID NO:), such as in paragraph [00134] on page 49. Applicant is reminded to check the entire disclosure to ensure that the application is in sequence compliance.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5-10 and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 6, 10, 16-17 and 21-24 of copending Application No. 10/481,642 ('642 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '642 application contains claims drawn to an immunizing composition comprising a dendritic polymer, built on a core molecule, which is at least difunctional so as to provide branching and containing up to 16 terminal functional groups to which an antigenic peptide of APP is covalently attached, and a method of eliciting an immune response comprising administering said immunizing composition, and which are species that would render obvious the instantly recited claims. For example, claim 6 of the '642 application recites that the amyloid β polypeptide comprises the amino acid sequence of SEQ ID NO: 5 (which is EFRH), which is a species that would render obvious the APP polypeptide recited in instant claim 5, for example, (SEQ ID NO: 5 of the instant application) which is the sequence VKMDA**EFRH**. Additionally, the '642 application recites limitations very similar to the instant claims such that the claims of the instant application would be rendered obvious. For example, the following claims of the '642 application recite nearly identical limitations of the instant application: the dendritic polymer contains eight terminal functional groups (claim 2 of '642, instant claim 3); the core molecule is lysine (claim 10 of '642, instant claim 8); the antigenic peptide comprises two epitopes of the deposit-forming polypeptide (claim 16 of '642, instant claim 6); the two epitopes are identical (claim 17 of '642, instant claim 7); the product further comprising a molecule having adjuvant properties (claim 21 of '642, instant claim

9); encapsulation in a liposome (clam 22 of '642, instant claim 10); method of eliciting immune response (claim 24 of '642, instant claim 15). Accordingly, the claims of the '642 application would render obvious instant claims 1-3, 5-10 and 15.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 11 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 11 of copending Application No. 11/475,247 ('247 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '247 application contains claims drawn to a pharmaceutical composition comprising a papillomavirus-like particle (PVLP) displaying an epitope of β-amyloid, wherein the epitope is EFRH (SEQ ID NO: 1 of '247), and which are species that would render obvious the immunizing composition comprising a viral display vehicle displaying the β-amyloid amino acid sequence VKMDAEFRH (SEQ ID NO: 5) instantly claimed. For example, PVLP is a species of "viral display vehicle", the instant SEQ ID NO: 5 encompasses the sequence EFRH, and the '247 application recites that the compositions elicits the production of antibodies, thus it is an immunizing composition. Accordingly, claims 11 and 14 are rendered obvious by the '247 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 11, 12 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3 and 10 of copending Application No. 11/073,526 ('526 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '526 application contains claims drawn to a pharmaceutical composition comprising a virus particle displaying an epitope of Aβ for eliciting antibody production which would render obvious the instantly claims immunizing composition comprising a viral display vehicle displaying an AβPP epitope. The '526 application recites that the virus is a bacteriophage (claim 3), thus rendering obvious instant claim 12. The '526 application further recites that the Aβ epitope comprises EFRH (claim 10), which would render obvious the AβPP epitope comprising VKMDAEFRH of instant claim 14. Accordingly, instant claims 11, 12 and 14 are rendered obvious by co-pending application '526.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects

for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 01/53457 A2 by Srivastava, filed January 18, 2001, priority to January 21, 2000, as evidenced by Vassar et al. (*Science*, 1999; 286: 735-741).

The claims are drawn to an immunizing composition comprising an antigenic product which induces an immune response against the β-secretase cleavage site of amyloid precursor protein (APP) and a pharmaceutically acceptable carrier, diluent, excipent, adjuvant, or auxiliary agent (claim 1). The claims are further drawn to a method for inducing an immune response against the β-secretase cleavage site of APP comprising administering the composition of claim 1 to a subject in need thereof, thereby inhibiting the formation of amyloid β (claim 15).

Srivastava teaches compositions comprising antigenic peptides associated with neurodegenerative diseases and disorders, such as Alzheimer's disease, which can be used as vaccines to protect against and/or treat such diseases and disorders (see paragraph spanning pp. 7-8). Srivastava discloses that the antigenic peptides may comprise amino acid sequences derived from APP proteins known to be associated with AD, or fragments thereof (see p. 9, lines 28-30). For example, Srivastava teaches that peptide fragments of a mutant APP comprising a mutation at codon 670 or 671 may be used, which are commonly known as the Swedish-type mutation (see Vassar et al., p. 735 3rd column and Figure1 on p. 736), and which would comprise the β-secretase cleavage site of APP. Additionally, Srivastava teaches the use of immunostimulatory adjuvants and carrier molecules for the antigenic composition (see pp. 32-34).

Individuals with Alzheimer's disease would meet the limitation of a "subject in need thereof", hence administration of the antigenic composition disclosed by Srivastava, which meets the limitations of instant claim 1, would inherently lead to the induction of an immune response against the β-secretase cleavage site of APP and block β-secretase cleavage of APP, and would thereby inhibit the formation of amyloid β, thus meeting the recited limitations of instant claim 15. Therefore, the document by Srivastava anticipates instant claims 1 and 15.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,721,130 to Seubert et al., issued February 24, 1998.

Seubert teaches the production of antibodies specific for the amino-terminal fragment form of β-amyloid precursor protein (ATF-βAPP). Seubert teaches the use of polypeptides comprising the C-terminal ATF-βAPP sequence including the methionine residue, which would comprise residues at the N-terminal β-secretase cleavage site of βAPP, for preparation of the antibodies (see column 6, line 48 – column 7, line 15). For example, Seubert discloses polypeptide sequences comprising ISEVKM (SEQ ID NO: 3) and KTEEISEVKM (SEQ ID NO: 9) coupled to an immunogenic carrier, such as serum albumin or KLH, and used in the production of specific antibodies (see column 7, lines 16-20). Such immunogenic carriers are recognized in the art as being pharmaceutically acceptable adjuvants. Accordingly, Seubert anticipates instant claim 1.

Claims 1-11 and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/72880 A2 by Schenk et al., published December 7, 2000.

Schenk teaches an immunizing composition comprising a fusion polypeptide, designated as pBx6, containing APP amino acid residues 592-695, and an adjuvant and used to immunize PDAPP transgenic mice (see paragraph spanning pp. 62-63). Because residues 670/671 of APP are noted to be the β-secretase cleavage site of APP (see p. 13, lines 32-33), APP polypeptide taught by Schenk containing residues 592-695 would comprise the β-secretase cleavage site of APP as well as residues 1-8 of instant SEQ ID NO: 1 and instant SEQ ID NO: 5, thus meeting recited limitations of instant claims 1, 4-5, 11 and 13-14. Additionally, PDAPP transgenic mice overexpress APP and develop Alzheimer's-like neuropathology, such as aggregated amyloid plaques in their brains. Thus, PDAPP mice would meet the limitation of "a subject in need thereof" recited in the immunization method of instant claim 15. The administration of such an immunizing composition to a subject in need thereof would induce an immune response against the β-secretase cleavage site of AβPP which would be expected to inherently result in the blockade of β-secretase cleavage of AβPP and the inhibition of the formation of amyloid β.

Schenk also teaches that immunogenic peptides, such as fragments of Aβ or APP as above, can be presented by a virus as part of an immunogenic composition (see p. 16, lines 16-17), thus meeting a recited limitation of instant claim 11. Schenk also teaches that immunogenic peptides can be expressed as fusion proteins with a carrier peptide, such as a T helper cell epitope, which can serve to induce a helper T-

cell response against the carrier peptide. The induced helper T-cells in turn induce a B-cell (i.e. antibody) response against the immunogenic peptide (see p. 29, lines 20-28). Schenk discloses that the fusion proteins comprising the immunogenic peptide can then be linked to a core molecule, such as lysine, to form a multimer of fusion proteins. The multimer is represented by the formula 2^x, in which x is an integer from 1-5, preferably x is 1, 2 or 3 (see p. 30, lines 13-22). For example, when x is 3, such a multimer has eight fusion proteins linked to a core molecule, thus meeting recited limitations of instant claims 2 and 3 regarding the number of function groups. Schenk teaches an example of the MAP4 (Multiple Antigen Peptide) configuration, in which 4 identical peptides have been produced on the branched lysine-containing core structure (see paragraph spanning pp. 30-31). Schenk teaches that such multiplicity greatly enhances the responses of B cells (see p. 30, line 29). Accordingly, these teachings would anticipate limitations recited in instant claims 6 (overlapping APP epitopes), 7 (wherein the overlapping epitopes are identical), and 8 (core molecule is lysine). The T helper cell epitope, which would be part of the fusion peptide comprising the immunogenic peptide, would thus meet a limitation of instant claim 9, which recites that the composition further comprises a molecule having adjuvant properties joined to said dendritic polymer. Further, Schenk discloses that pharmaceutical compositions comprising the immunogenic peptides can be encapsulated in liposomes or micro particles for enhanced adjuvant effect (see p. 41, lines 29-33), thus meeting a recited limitation of instant claim 10. Accordingly, the document by Schenk anticipates instant claims 1-11 and 13-15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/72880 A2 by Schenk et al., published December 7, 2000, in view of Frenkel et al. (*Proc Natl Acad Sci USA*, 2000; 97(21): 11455-11459, listed on Applicant's IDS).

The claims are drawn to an immunizing composition comprising a viral display vehicle displaying on its surface an AβPP epitope spanning the β-secretase cleavage site of AβPP (claim 11), wherein the viral display vehicle is a filamentous bacteriophage (claim 12).

The teachings of Schenk are discussed above. Briefly, Schenk teaches an immunizing composition comprising an AβPP epitope spanning the β-secretase cleavage site of AβPP (see paragraph spanning pp. 62-63) and additionally teaches that

the immunogenic peptide can be presented by a virus as part of an immunogenic composition (see p. 16, lines 16-17). However, Schenk does not specifically disclose that the viral display vehicle is a filamentous bacteriophage.

Frenkel et al. teach an immunization procedure for the production of anti-aggregating β-amyloid antibodies based on filamentous phages displaying a particular epitope of β-amyloid (see p. 11455). Frenkel teaches that immunization with f88 or f3 filamentous phage displaying the sequence EFRH led to the production of high titers of serum antibodies which persisted for several months without any evidence of toxic effects (see Figures 2 and 3, and p. 11458, 1st column). Frenkel teaches that because of the high antigenicity of the phage, no adjuvant is required to obtain high affinity antibodies after a short immunization period of 3 weeks (see Abstract). Additionally, Frenkel notes that the availability of such antibodies opens up possibilities for the development of an efficient and long-lasting vaccination for the treatment of Alzheimer's disease (see Abstract).

It would have been obvious to one of skill in the art at the time the invention was made to select a filamentous bacteriophage as taught by Frenkel et al. for displaying the APP fragments disclosed by Schenk et al. as the specific viral display vehicle for an immunizing composition. The artisan would be motivated to make such a selection because Frenkel et al. teach that immunization with f88 and f3 filamentous phage displaying a particular epitope led to the induction of sustained high antibody IgG titers, thus requiring fewer immunizations over a shorter immunization period. The skilled artisan would likewise be motivated to use filamentous bacteriophages for the

expression of the desired APP epitope because Frenkel teaches that such virally-displayed peptides were immunogenic enough to negate the need for an additional adjuvants whilst still being non-toxic to the host, and that such peptide-displaying phage vaccines may be useful for potential Alzheimer's disease therapies. Such combination would be met with an expectation of success by the artisan based upon the successful results taught by Frenkel et al., demonstrating high antibody titers (Figure 2) that are sustained for several months (Figure 3). Thus, the combined references render the claimed invention obvious to the artisan at the time the invention was made.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on M-F 9AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard, Ph.D.
November 16, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER